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Subject:	Serial Nos. 08/358,627 and 08/465,712	**Date:**	September 19, 2000
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Message:

Dear Examiner Kerr:

Attached are the allowed claims we discussed.

Sincerely,

Timothy B. Donaldson/dmb

Timothy B. Donaldson
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ALLOWED CLAIMS
U.S. Patent Appln. Serial No. 08/358,627
Inventor: Jene-Pierre CHANGEUX et al.
Our Ref: 03495.0135-00000

1. An isolated DNA selected from the group consisting of:

(A) the sequence from about nucleotide -1125 to about nucleotide +38 as set forth in Figure 1 (SEQ ID NO. 22); and

(B) a sequence having promoter activity, which hybridizes to DNA complementary to said sequence (A) under stringent conditions, wherein said stringent conditions comprise a temperature of about 65°C and an SSC buffer concentration of about 0.1xSSC.

2. An isolated DNA, comprising the DNA as claimed in claim 1 operatively linked to a nucleotide sequence encoding a polypeptide.

3. An isolated DNA as claimed in claim 2, wherein the polypeptide is encoded by a reporter gene.

4. An isolated DNA as claimed in claim 3, wherein the reporter gene encodes β-galactosidase or Luciferase.

5. An isolated nucleic acid, which hybridizes to the nucleotide sequence (A) of claim 1 under said stringent conditions.

6. An isolated DNA, which is a sequence from about nucleotide -245 to about nucleotide -95 in Figure 1 (SEQ ID NO. 22).

7. An isolated DNA, consisting of the sequence from about nucleotide -824 to about nucleotide -245 in Figure 1 (SEQ ID NO. 22).

8. An isolated DNA consisting of the sequence from about nucleotide -135 to about nucleotide -103 in Figure 1 (SEQ ID NO. 22).

9. An isolated DNA consisting of the sequence from about nucleotide +16 to about nucleotide +36 in Figure 1 (SEQ ID NO. 22).

10. An isolated DNA selected from the group consisting of the sequence from about nucleotide -968 to about nucleotide +38, the sequence from about nucleotide -824 to about nucleotide +38, and the sequence from about nucleotide -245 to about nucleotide +38, as set forth in Figure 1 (SEQ ID NO. 22).

11. A recombinant vector containing the nucleotide sequence as claimed in claim 1.

12. A recombinant vector containing the nucleotide sequence of claim 2.

13. An isolated cell, comprising the vector as claimed in claim 12.

14. An isolated DNA having a sequence comprising the DNA of claim 1 operatively linked to a tumorigenic, oncogenic or immortalizing gene.

19. A cloned genomic DNA sequence encoding at least one exon of the mouse β2-subunit of neuronal nicotinic acetylcholine receptor, wherein said exon is selected from the group consisting of exon I, exon II, exon III, and exon IV.

21. Plasmid pSA9, Deposit I-1501 at the Collection Nationale de Cultures de Microorganismes.

22. Plasmid pEA5, Deposit I-1502 at the Collection Nationale de Cultures de Microorganismes.

23. Phage λβ2 nAchR, Deposit I-1503 at the Collection Nationale de Cultures de Microorganismes.

25. A macromolecular complex comprising a DNA as claimed in claim 1 or claim 19 and a protein.

26. A method of detecting a protein, which binds to a promoter, comprising incubating the DNA as claimed in claim 1 with a nuclear extract under conditions suitable to allow a protein in said nuclear extract to bind to said DNA to form a DNA/protein complex, and detecting said DNA/protein complex.

27. A method as claimed in claim 26 wherein the DNA is the sequence of oligonucleotide E-D, Mut-E, or S-E.

33. An isolated DNA fragment having a regulatory or coding sequence of the mouse β2-subunit of neuronal nicotinic acetylcholine receptor obtainable by cutting the DNA of the phage of claim 23 with restriction enzyme or mechanical shearing.

34. An isolated DNA, comprising the DNA in claim 1, operatively linked to a heterologous DNA sequence encoding a polypeptide.

36. A cell line, comprising in its genome a foreign nucleotide sequence comprising the DNA as claimed in claim 34.

40. An isolated DNA selected from the group consisting of:

(A) the sequence from about nucleotide -1125 to about nucleotide +38 as set forth in Figure 1 (SEQ ID NO. 22); and

(B) a sequence having promoter activity, which hybridizes at 65°C in 0.1XSSC to DNA complementary to said sequence (A).

42. A method for isolating a protein, which binds to a promoter, comprising incubating the DNA as claimed in claim 1 with a nuclear extract under conditions suitable to allow a protein in said nuclear extract to bind to said DNA to form a DNA/protein complex, and isolating said protein, which binds to said promoter.

43. An isolated DNA having the sequence set forth in Figure 1 (SEQ ID NO. 22).

44. An isolated DNA having a sequence from about nucleotide -1125 to about nucleotide +38 as set forth in Figure 1 (SEQ ID NO. 22).

45. An isolated DNA, comprising the DNA as claimed in claim 44 operatively linked to a nucleotide sequence encoding a polypeptide.

46. An isolated DNA as claimed in claim 45, wherein the polypeptide is encoded by a reporter gene.

47. An isolated DNA as claimed in claim 46, wherein the reporter gene encodes β-galactosidase or Luciferase.

48. An isolated nucleic acid, comprising a sequence complementary to a nucleotide sequence of claim 44.

49. A recombinant vector containing the nucleotide sequence as claimed in claim 44.

50. A recombinant vector containing the nucleotide sequence of claim 45.

51. An isolated cell, comprising the vector as claimed in claim 50.

52. An isolated DNA having a sequence comprising the DNA of claim 44 operatively linked to a tumorigenic, oncogenic or immortalizing gene.

53. A method of detecting a protein, which binds to a promoter, comprising incubating the DNA as claimed in claim 44 with a nuclear extract under conditions suitable to allow a protein in said nuclear extract to bind to said DNA to form a DNA/protein complex, and detecting said DNA/protein complex.

55. An isolated DNA, comprising the DNA in claim 44, or a fragment of the DNA in claim 44, wherein said fragment has promoter activity and is operatively linked to a heterologous DNA sequence encoding a polypeptide.

56. A cell line comprising in its genome a nucleotide sequence comprising the DNA as claimed in claim 55.

57. A method for isolating a protein, which binds to a promoter, comprising incubating the DNA as claimed in claim 44 with a nuclear extract under conditions suitable to allow a protein in said nuclear extract to bind to said DNA to form a DNA/protein complex, and isolating said protein, which binds to said promoter.

59. An isolated DNA having at least one point mutation in a nucleotide sequence from about nucleotide -1125 to about nucleotide +38 as set forth in Figure 1 (SEQ ID NO. 22), wherein the at least one point mutation is localized between nucleotide -118 and nucleotide -113.

60. An isolated DNA having at least one point mutation in a nucleotide sequence from about nucleotide -1125 to about nucleotide +38 as set forth in Figure 1 (SEQ ID NO. 22), wherein the at least one point mutation is localized between nucleotide +18 and nucleotide +35.

Allowed claims
U.S. Patent Appln. Serial No. 08/465,712
Inv ntor: Jene-Pierre CHANGEUX et al.
Our Ref: 03495.0135-01000

15. A transgenic mouse all of whose germ cells and somatic cells contain a DNA sequence comprising a promoter of the β2-subunit of neuronal nicotinic acetylcholine receptor having the sequence from about nucleotide -1125 to about nucleotide +38 as set forth in Figure 1 (SEQ ID NO. 22) operatively linked to a nucleotide sequence encoding a heterologous polypeptide, wherein said polypeptide is expressed in neurons of said transgenic mouse, and wherein the DNA was introduced into the mouse or an ancestor of the mouse at an embryonic stage.

16. A process for the *in vitro* culture of mammalian cells, comprising isolating said cells from a mouse as claimed in claim 15 and culturing said isolated cells *in vitro*.

39. A transgenic mouse, generated by providing a first transgenic mouse as claimed in claim 49, and crossing said first mouse with a second mouse, wherein nicotine binding in the brain of said transgenic mouse is reduced by at least approximately 50% as compared to a wild-type mouse.

41. A transgenic mouse as claimed in claim 48, wherein said reporter gene encodes luciferase or β-galactosidase.

46. A neuronal cell line produced from the mouse as claimed in claim 15.

47. A neuronal cell line produced from the mouse as claimed in claim 49.

48. The transgenic mouse of claim 15, wherein the nucleotide sequence encoding a heterologous polypeptide is a reporter gene.

49. A transgenic mouse all of whose somatic cells and germ cells contain a homozygous disruption of the endogenous β2-subunit of the neuronal nicotinic acetylcholine receptor, wherein said homozygous disruption results in the absence of expression of the β2-subunit of the neuronal nicotinic acetylcholine receptor and a lack of inward current activity in anterior thalamic neurons in response to a nicotinic acetylcholine receptor agonist.